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Nina Rautonen

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STEPTOE & JOHNSON LLP
1330 CONNECTICUT AVENUE, N.W.
WASHINGTON, DC 20036

EXAMINER

MACAULEY, SHERIDAN R

ART UNIT

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1651

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

1. A response and amendment were received and entered on March 29, 2010. All evidence and arguments have been fully considered. Claims 25-27 are cancelled. Claims 1-24 and 28-39 are pending. Claims 1-21 and 29-39 are withdrawn due to a previous requirement for restriction. Claims 22-24 and 28 are examined on the merits in this Office action.

Specification

2. Applicant's amendment to the specification is acknowledged. However, the specification is objected to because it appears that applicant has amended the title of the invention to contain a typographical error. Applicant has amended the title of the invention to "A Method of Increasing the Amount of COX-1 mDRNA in a Subject". However, the term "mDRNA" is not in the specification and, based on applicant's remarks, it appears that applicant intended to recite "mRNA". It is suggested that applicant amend the title of the specification to "A Method of Increasing the Amount of COX-1 mRNA in a Subject" or another appropriate phrase. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. Rejections under 35 USC 112, second paragraph have been withdrawn due to applicant's amendment.

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4. Rejections under 35 USC 112, first paragraph have been withdrawn due to applicant's arguments (see applicant's remarks filed on March 27, 2010, p. 10, par. 3 and Appendix A).

Claim Rejections - 35 USC § 102

5. Rejections under 35 USC 102 have been withdrawn due to applicant's amendment.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

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were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins (US 2002/0006432 A1, cited in prior action) in view of Van Der Mei (J. Med. Microbiol. 49:713-718, cited in prior action). Claim 22 recites a method of treating and/or preventing the side-effects associated with the administration of nonsteroidal anti-inflammatory drugs, which method comprises administering to the patient an effective amount of a microorganism, which microorganism at least increases the amount of a COX-1 mRNA in at least one cell of the subject, wherein the microorganism *Bifidobacterium* sp. 420. Claims 23 and 24 recite the method according to claim 22, wherein the microorganism modifies the amount of a thither cyclooxygenase mRNA in said cell and wherein the microorganism increases the amount of a COX-1 mRNA in said cell, whilst simultaneously decreases the amount of a COX-2 mRNA in said cell.

10. Collins teaches a method of treating a subject by administering bacteria of the genus *Bifidobacterium* to a subject (abstract). The reference teaches that the bacteria may be administered in conjunction with NSAIDs (p. 4, par. 76). The functions recited in the claims, i.e., the effect on mRNA, would be inherent to the method of Collins. The reference does not specifically teach the use of *Bifidobacterium* sp. 420 in the method of using the bacteria.

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11. Van Der Mei teaches the use of various strains of bacteria, including *Bifidobacterium* sp. 420, in methods for assessing their probiotic effects (abstract).

12. At the time of the invention a method of administering the bacterium recited in the claims was known, as taught by Collins. It was further known that *Bifidobacterium* sp. 420 was an available species of bacteria, as taught by Van Der Mei, and further that the species may have probiotic effects. One of ordinary skill in the art would have been motivated to use *Bifidobacterium* sp. 420 in the method of Collins because Collins teaches that any species of *Bifidobacterium* with probiotic effects may be used in the method, and further teaches methods for testing such strains for probiotic effects (p. 2, par. 14-15, p. 4, par. 81-83). One would therefore have recognized that *Bifidobacterium* sp. 420 could have been tested for such effects and used in the methods of Collins. One of ordinary skill in the art would have had a reasonable expectation of success in using the strain in the methods of Collins because Collins teaches the use of using multiple *Bifidobacterium* strains in the methods. It would therefore have been obvious at the time of the invention to combine the teachings discussed above to arrive at the claimed invention.

13. Claims 22-24 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins (US 2002/0006432 A1, cited in prior action) in view of Van Der Mei (J. Med. Microbiol. 49:713-718, cited in prior action), as applied to claims 22-24 above, and further in view of Zimmer (US 5,501,857, cited in prior action) or Chen et al. (US 2001/0014322 A1, cited in prior action). Claims 22-24 are described above. Claim 28

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recites method according to claim 22, wherein the subject is further administered with an effective amount of betaine or a pharmaceutically acceptable salt thereof or a betaine replacement compound, wherein said betaine replacement compound is any methyl donor.

14. Collins teaches a method of treating a subject by administering bacteria of the genus *Bifidobacterium* to a subject (abstract). The reference teaches that the bacteria may be administered in conjunction with NSAIDs (p. 4, par. 76). The functions recited in the claims, i.e., the effect on mRNA, would be inherent to the method of Collins. The reference does not specifically teach the use of *Bifidobacterium* sp. 420 in the method of using the bacteria.

15. Van Der Mei teaches the use of various strains of bacteria, including *Bifidobacterium* sp. 420, in methods for assessing their probiotic effects (abstract).

16. As discussed in the rejections above, it would have been obvious to combine the teachings of Collins and Van Der Mei to arrive at nearly all aspects of the claimed invention. However, the references do not specifically teach the addition of a betaine or betaine replacement compound to the composition comprising the bacteria.

17. Zimmer and Chen teach compositions comprising probiotic bacteria, such as a *Bifidobacterium*, and choline (a betaine replacement compound; see Zimmer, abstract, col. 12, example 1; and Chen, abstract, p. 3, par. 21).

18. At the time of the invention, a method of administering a bacterium such as that recited in the claims was known, as taught by Collins and Van Der Mei. It was further known that such bacteria could have been administered with a betaine replacement

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compound, as taught by Zimmer and Chen. One of ordinary skill in the art would have been motivated to combine the teachings by administering the betaine replacement compound in the method of Collins because both Zimmer and Chen teach that it is desirable to administer bacteria in combination with such components. One of ordinary skill in the art would have had a reasonable expectation of success in combining the components in a method such as that recited in the claims because Zimmer and Chen both teach that betaine replacement compounds are compatible with the bacteria. It would therefore have been obvious at the time of the invention to combine the teachings discussed above to arrive at the claimed invention.

19. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Response to Arguments

20. Applicant's arguments filed March 29, 2010 have been fully considered but they are not persuasive. Applicant argues that the cited references do not render obvious the claimed invention. Specifically, applicant argues that, since Collins teaches the administration of a different strain of probiotic bacteria than is recited in the instant claims, the claims are not rendered obvious by the cited prior art. However, the strain recited in the claims *Bifidobacterium* sp. 420, was known in the art at the time of the invention, as taught by Van Der Mei. The reference further teaches that the species may have probiotic effects. One of ordinary skill in the art would have been motivated to

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use *Bifidobacterium* sp. 420 in the method of Collins because Collins teaches that any species of *Bifidobacterium* with probiotic effects may be used in the method, and further teaches methods for testing such strains for probiotic effects (p. 2, par. 14-15, p. 4, par. 81-83). One would therefore have recognized that *Bifidobacterium* sp. 420 could have been tested for such effects and used in the methods of Collins. Therefore, the instant claims are rendered obvious by the prior art, as discussed in detail in the rejections above.

21. Although applicant argues that the strain provides a specific advantage over the strain used by Collins, in that the strain used in the instantly claimed method has direct effects on epithelial COX gene expression, it is noted that the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new. Thus the claiming of a new use, functions or unknown property that is inherently present in the prior art does not necessarily make the claim patentable (MPEP 2112). In the instant case, the bacterial strain (*Bifidobacterium* sp. 420) was known in the prior art, and the composition was known to be useful as a probiotic. Thus, the explanation of the mechanisms by which the probiotic composition is effective does not render the claim patentable. Furthermore, even if the results cited by applicant were found to provide a benefit over the compositions of the prior art, applicant's evidence of surprising results is not commensurate with the scope of the claims. Applicant asserts that the *Bifidobacterium* sp. 420 composition has direct effects on epithelial COX gene expression; however, the claims are directed to any increase in the amount of COX-1

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mRNA in any cell of the subject. Therefore, applicant's arguments regarding the unexpected advantages of the claimed method are not found to be persuasive.

22. Applicant further argues that Collins does not provide motivation to use another strain of *Bifidobacterium* in the method disclosed therein because the reference is primarily directed to the use of a specific strain of *Bifidobacterium* that is not the strain recited in the instant claims. However, Collins teaches that any species of *Bifidobacterium* with probiotic effects may be used in the method (preferably, one that effects changes in an immunological marker, p. 2, par. 14-15), and further teaches methods for testing such strains for probiotic effects (p. 4, par. 81-83). One of ordinary skill in the art would have therefore recognized that the method of Collins may be used with different types of probiotic bacteria, particularly within the *Bifidobacterium* genus, and would have looked towards the prior art teaching other species of probiotic *Bifidobacterium* species, such as Van Der Mei, for other species to assess for use in the method. Although applicant further argues that Van Der Mei is not relevant to the teachings of Collins because the two references teach the use of probiotics for different purposes, it is noted that Collins teaches that *Bifidobacterium* species are useful for use in the method and further teaches methods to assess their usefulness for administration in the method taught therein. Regardless of whether Van Der Mei teaches the use of the probiotic *Bifidobacterium* species taught therein for a different purpose, one of ordinary skill in the art would have recognized that a *Bifidobacterium* species could have been selected for use from a finite number of members of the species, and would further have been motivated to select the species taught in the Van Der Mei reference because it

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had previously been used as a probiotic. Therefore, applicant's argument has not been found to be persuasive.

23. Therefore, applicant's arguments have been fully considered, but they have not been found to be persuasive.

Conclusion

No claims are allowed.

24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHERIDAN R. MACAULEY whose telephone number is

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(571)270-3056. The examiner can normally be reached on Mon-Thurs, 7:30AM-5:00PM EST, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRM

/Ruth A. Davis/

Primary Examiner, Art Unit 1651